Screening and Diagnosis of Gestational Diabetes Mellitus Using 75-g Oral Glucose Tolerance Test Following the WHO, ADA, and IADPSG Criteria

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Abstract

Aim: We aim to compare the World Health Organization (WHO), American Diabetes Association (ADA), and the International Association of Diabetes and Pregnancy Study Groups (IADPSG) criteria to diagnose gestational diabetes mellitus in Metro Manila, Philippines.

Materials and methods: We used a retrospective cohort study design and reviewed 75-g oral glucose tolerance test results of 919 pregnant women at selected hospital-based and free-standing laboratories in Metro Manila. We used three criteria for diagnosing GDM namely, WHO (fasting: 7.0 mmol/L; 2-hour value: 11.1 mmol/L), ADA (fasting: 5.28 mmol/L; 1-hour: 10 mmol/L; 8.61 mmol/L), or IADPSG (fasting: 5.11 mmol/L; 1 hour: 10 mmol/L; 2-hour value: 8.5 mmol/L) and computed and compared their diagnostic sensitivity, diagnostic specificity, positive predictive value (PPV) and negative predictive value (NPV).

Results: Following the WHO criteria, we found 48 GDM patients; using ADA criteria, 150 have GDM; and using IADPSG criteria, 269 women have GDM. Applying the IADPSG criteria to the population would increase the rate of GDM from 5.22% (WHO) to 16.32% (ADA) to 29.27%. Giving the highest prevalence rate, we used IADPSG criteria as the standard to compute for diagnostic sensitivity, diagnostic specificity, NPV and PPV. Results showed that the diagnostic sensitivity of OGTT using ADA criteria is 55.97%, which is higher than using the WHO criteria (17.91%). ADA criteria also has a higher NPV of 84.66% as compared with WHO criteria NPV of 74.74%. In terms of diagnostic specificity, both ADA and WHO criteria have 100% specificity.

Conclusions: The use of IADPSG criteria instead of ADA and WHO criteria would result in a considerable increase in the prevalence rate of GDM, which would lessen cases of misdiagnosis. Further, standardizing the criteria for diagnosis will prevent pregnancy complications due to GDM. A single global criterion for the diagnosis of GDM is a must to strengthen its diagnosis and protect both the mother and the baby from complications.

Keywords: Filipinos; Gestational diabetes; OGTT; World Health Organization; American Diabetes Association; International Association of Diabetes and Pregnancy Study Groups

Introduction

Gestational diabetes mellitus (GDM) is one of the most common medical complications during pregnancy with its prevalence being comparable to the rate of impaired glucose tolerance (IGT), obesity, and type 2 diabetes mellitus (T2DM) [1,2]. It is defined as any degree of carbohydrate intolerance resulting in hyperglycemia with onset or first recognition during pregnancy [3].

GDM prevalence is increasing worldwide, particularly in Asian countries [1,4,5]. In the Philippines, very few studies have been done about GDM. The only available data on the prevalence of GDM in the Philippines is the study done by Litonjua et al in 1996. In this study, they identified that the GDM prevalence in the Philippines is 14% [6]. A more recent was done but with limited scope of population, that is covering the University of Santo Tomas Hospital-Clinical Division (USTH-CD) only. In the study, they identified that the prevalence of

GDM at the USTH-CD was 7.5% and GDM was associated with increasing body mass index (BMI), family history of diabetes, and use of hormonal [7]. With limited available studies on GDM, as well as the challenge of having various criteria to diagnose GDM in the Philippines, increase the burden of the condition.

Although normal glucose metabolism is restored after delivery, GDM poses short and long-term complications to both the mother and the baby such as birth trauma, hypertension, macrosomia, and subsequent development of T2DM [5,8,9] Recognizing the adverse complications the mother and baby are at risk of, it is critical to have a good diagnostic strategy to detect the condition.

Current test done to diagnose GDM is oral glucose tolerance test (OGTT) and results are commonly interpreted using the criteria set by either the World Health Organization (WHO), American Diabetes Association (ADA), or International Association of the Diabetes and Pregnancy Study Groups (IADPSG) [6,10,11]. Three criteria are available for the diagnosis of GDM and selection of criterion is dependent on the laboratory protocol or on the preference of the obstetrician-gynecologist. Ideally, the choice of criteria to use should

be population dependent. Most countries follow either the WHO or ADA criteria. Recently, IADPSG criterion was introduced. Since this criterion was based on Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study, studies have emerged to compare the IADPSG criterion with WHO criterion in specific populations. In most instances, the use of the new IADPSG guidelines increased the prevalence of GDM. But increasing the prevalence of GDM does not necessarily mean improved pregnancy outcomes [12]. In the Philippines, two criteria are endorsed by two recognized societies in the country, namely, the UNITE for Diabetes Philippines endorsed the IADPSG criteria, and the Philippine Obstetrical and Gynecological Society (POGS) endorsed the WHO guideline [13].

With increasing number of available criteria to use in the diagnosis of GDM, the main challenge now is which criteria to follow. The lack of a standard protocol to diagnose GDM led to increasing number of undiagnosed, misdiagnosed and untreated cases. However, using, for example, IADPSG criteria would reverse the problem of misdiagnosis. But this may also pose a risk to the pregnant women and the infant in terms of therapeutic management that is, giving treatment to women with no GDM but tested positively with the criteria used.

The aim of our study was to compare WHO, ADA, and IADPSG criteria in diagnosing GDM using the 75-g OGTT in the Filipino population. Moreover, we determined which among the criteria is the most diagnostically sensitive and specific in the Filipino population lessening cases of misdiagnosis (false negative and false positive results).

Materials and Methods

This was a retrospective cohort study involving women who underwent screening for GDM at selected hospital-based and free-standing laboratories around Metro Manila from January to December 2016. The sample size for this study was calculated using the free sample size calculator from Raosoft (Rasosoft, Inc., USA). A population size of 356,541, 95% confidence interval, and a 5% margin of error was used for the computation. The population size was based on the number of pregnant women receiving pre-natal check-ups in the National Capital Region based on the 2016 Field Health Service Information System Annual Report of the Epidemiology Bureau of the Department of Health. Based on the results of the computation, a baseline sample population composing of 384 pregnant women is needed; however, we were able to extend our collection up to 919 pregnant women which increases the power of our study.

Ethical clearance in the conduct of the study was obtained from the University of Santo Tomas Graduate School Ethics Review Board as part of the project entitled, "Blood and placental gene expression analysis in Gestational Diabetes Mellitus: potential identification of early biomarkers." Names of the pregnant women included in the study were de-identified and only the OGTT results of the patients were utilized in the study.

Only pregnant women free of recognizable diabetes mellitus prior to pregnancy and who have undergone 75-g OGTT in the selected laboratories were included in the study. Diagnosis of GDM during the study period was based on 75-g OGTT using criteria of either WHO, ADA or IADPSG (Table 1). In this study, we used the three criteria to diagnose GDM and compare the percentage of GDM prevalence following each criterion.

Glucose measure	WHO*	ADA**	IADPSG *
Fasting serum glucose	7.0	5.28	5.11
1-hour serum glucose	N/A	10.0	10.0
2-hour serum glucose	11.1	8.61	8.5

Table 1: WHO, ADA, and IADPSG Criteria for Diagnosing GDM using 75-g OGTT Results (in mmol/L). Legend: N/A-not applicable; *any one value meeting the threshold is considered GDM; **any two values meeting the threshold is considered GDM.

We computed for the prevalence of GDM using the three criteria (P=number of pregnant women with GDM over total number of samples multiplied to 100). The criteria giving the highest prevalence of GDM was used as the standard to compute for diagnostic specificity and sensitivity, PPV and NPV of the two other criteria.

Results

Overall, 919 pregnant women of gestational age were eligible for the study. Following the WHO criteria, we found 48 GDM patients; using ADA criteria, 150 participants GDM patients; and using IADPSG criteria, 269 women have GDM. Applying the IADPSG criteria to the population would increase the rate of GDM from 5.22% (WHO) to 16.32% (ADA) to 29.27%. Figure 1 below shows the graphical representation of the increasing prevalence of GDM using WHO, ADA, and IADPSG criteria.
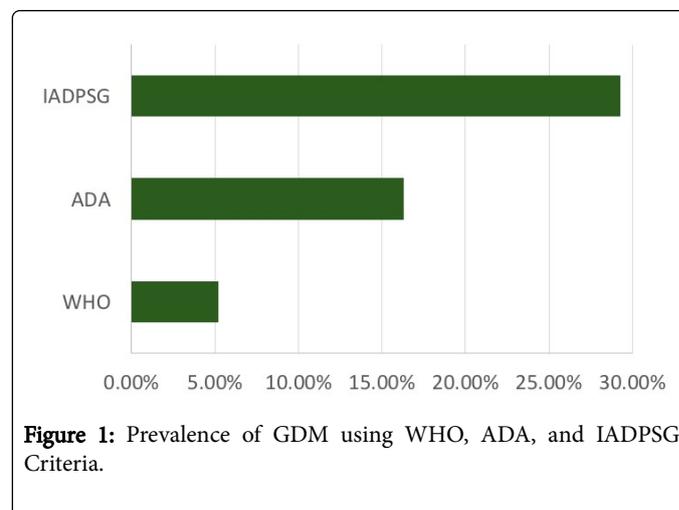

Figure 1: Prevalence of GDM using WHO, ADA, and IADPSG Criteria.

Giving the highest prevalence rate, we used IADPSG criteria as the standard to compute for diagnostic sensitivity, diagnostic specificity, NPV, and PPV. Table 2 below summarizes the number of GDM cases diagnosed using either WHO or ADA criteria in reference to IADPSG criteria.
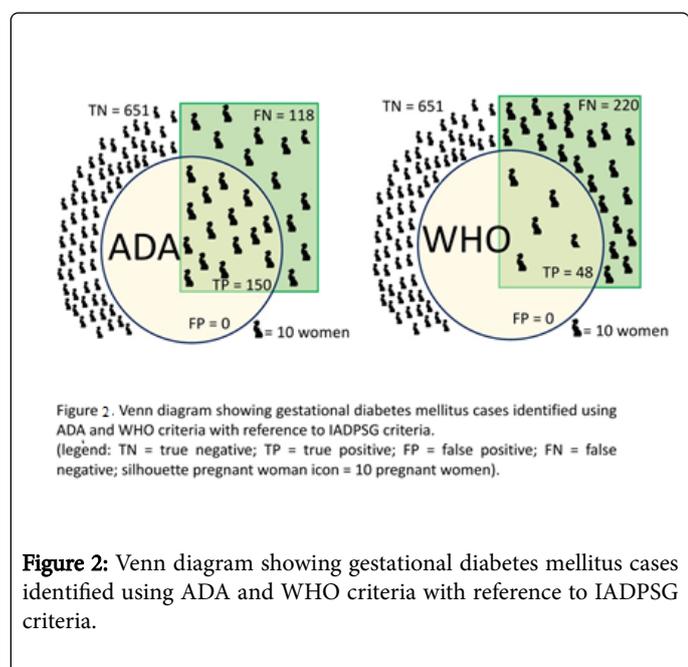
The values in Table 2 is further represented using Figure 1 below. In Figure 2, we can see that following the ADA criteria, only 150 pregnant women (overlap of circle and rectangle) were diagnosed to have GDM, thus, missing about 118 pregnant women. Moreover, using WHO, only 48 women have GDM (overlap of circle and rectangle) and about 220 women have been misdiagnosed. With these values, we were able to compute that the diagnostic sensitivity of OGTT using ADA criteria is 55.97%, which is higher than using the WHO criteria (17.91%). ADA

criteria also has a higher NPV of 84.66% as compared with WHO criteria NPV of 74.74%. In terms of diagnostic specificity, both ADA and WHO criteria have 100% specificity.

Total Number of Respondents	Tested Positive using:			Number of:							
	ADA	WHO	IADPSG	ADA				WHO			
				TP	TN	FP	FN	TP	TN	FP	FN
919	150	48	269	150	651	0	118	48	651	0	220

Table 2: Frequency of true positive, true negative, false positive and false negative results using ADA and WHO criteria with reference to IADPSG Criteria. Legend: TP-true positive; TN-true negative; FP-false positive; FN-false negative.

Figure 2. Venn diagram showing gestational diabetes mellitus cases identified using ADA and WHO criteria with reference to IADPSG criteria.
(legend: TN = true negative; TP = true positive; FP = false positive; FN = false negative; silhouette pregnant woman icon = 10 pregnant women).

Figure 2: Venn diagram showing gestational diabetes mellitus cases identified using ADA and WHO criteria with reference to IADPSG criteria.

Discussion

GDM is a pregnancy complication affecting both the mother and the baby even after delivery. Adverse complications for the mother such as preeclampsia, still birth, abortion, early delivery, caesarean delivery, risk for cardiovascular diseases and T2DM and others, and for the baby such as macrosomia, fetal malformation, obesity, risk for T2DM, and among others have been noted [11,14,15]. And to prevent these complications, a good diagnostic criterion that will screen the mother early during pregnancy is needed.

75-g OGTT is the most common laboratory test done to detect GDM. And various criteria are available to diagnose GDM using the OGTT results. In our study, we compared three criteria such as WHO, ADA, and IADPSG criteria. Being able to identify high cases of GDM, IADPSG was used as the basis for comparing the diagnostic sensitivity and specificity of ADA and WHO criteria. Using the IADPSG criteria as standard in this study does not mean that it is the best criteria to use in the Filipino population because pregnancy outcomes observation is not included in our study. Both the benefits and drawback of using this criteria to the population is not yet been studied. Similar results in terms of increased GDM prevalence have been obtained by previous studies when using the IADPSG criteria. For instance, in the study done at Hospital Clinico San Carlos (St. Carlos Hospital) involving a total of 3,276 pregnant women, the use of IADPSG criteria resulted in a GDM prevalence rate of 35.5% compared to Carpenter-Coustan (CC) Criteria [12]. In the study, they were able to note improvement in some pregnancy outcomes such as decrease rate of gestational hypertension, decrease cases of caesarean section, decrease number of babies small or large for gestational age, less cases of babies with APGAR score less than seven, and less cases of admission to neonatal intensive care unit. Another study focused on the prevalence of GDM and its risk factors and utilized IADPSG criteria and compared with WHO criteria in diagnosing GDM [16]. The study included a total of 18,589 pregnant women but only 2,953 had 75-g OGTT and 781 used oral glucose challenge test (OGCT) instead. With adjusted prevalence of GDM because of using OGCT results only in some patients, the use of IADPSG criteria gave a prevalence of 9.3% compared to 8.1% using WHO criteria. Moreover, in another study, IADPSG criteria was compared with Canadian Diabetes Association (CDA) criteria. Using the IADPSG criteria, they were able to identify 10.3% of 5,429 women with GDM as compared with 3.2% GDM cases identified using CDA criteria [17]. In the study of Rajput et al., in 2015, they compared IADPSG criteria with ADA and WHO criteria. Their results are similar with the results of our study were most of GDM cases have been identified by IADPSG criteria. However, they mentioned that although IADPSG, as well as WHO, was able to detect more cases of GDM, the two criteria did not predict adverse pregnancy outcomes [18]. The use of IADPSG criteria has been accepted by several international and national bodies such as the WHO, ADA, The Endocrine Society, and some countries such as India, Brazil, Italy, Germany, Austria, Canada, Japan, and Australia. However, it was rejected by American College of Obstetrics and Gynecologists, the National Institutes of Health Panel (USA), and of Spain and New Zealand [10]. Increased detection of GDM using IADPSG has both benefits and limitations. Limitations would be in terms of the effect in the mother and the baby after therapeutic management. Current therapy given to pregnant women with hyperglycemia include insulin therapy or an oral antidiabetic agents such as glyburide and metformin [19]. Studies have shown various placental, fetal and maternal changes in GDM patients treated with either insulin or oral antidiabetic agents [19-21]. For instance, babies borne from GDM mothers who had exogenous insulin are heavier compared to diet controlled GDM mothers, and increased fetal weights have been associated with adverse fetal and maternal outcomes [20]. Another study where the use of metformin was compared with insulin therapy, their meta-analysis resulted to metformin being comparable with the effects of insulin and with less adverse neonatal outcomes and more benefits to the mother such as inhibition of abnormal maternal weight gain [21].

In comparing ADA and WHO criteria, the ADA criteria is more diagnostically sensitive and has a greater NPV than WHO. With the ADA criteria having a higher sensitivity than that of WHO, this equates to the test having a higher probability to recognize an individual who have the disease as positive. A highly sensitive test means that there are few false negative results, and thus fewer cases of disease are missed. The ADA criteria were able to identify about 150 respondents as positive for GDM while the WHO criteria were only able to identify around 48 respondents as positive for GDM. There was about three-fold increase in the number of identified GDM cases

between WHO and ADA shown in our study. But still with IADPSG criteria included in the options of criteria to use in the diagnosis of GDM, IADPSG criteria gave the highest prevalence of GDM. By being able to diagnose more women with GDM, the ADA criteria have a greater potential of preventing adverse maternal and perinatal outcomes such as fetal macrosomia, severe obesity, neonatal metabolic disturbance, still-birth pregnancies, fetal malformation, and among others [22]. In a meta-analysis article focused on the prevalence of GDM in Eastern and Southeastern Asia, articles included utilized several criteria in the diagnosis of GDM such as ADA, Australian Diabetes in Pregnancy Society (ADIPS), CC, IADPSG, International Classification of Diseases (ICD), Japan Society of Obstetrics and Gynecology (JSOG), National Diabetes Data Group (NDDG), and WHO. The overall prevalence of GDM, regardless of diagnostic standards/criteria, is 10.07%. But taking into consideration the criteria of diagnosis, IADPSG criteria gave the highest prevalence of 13.77% [23].

The use of IADPSG Criteria instead of ADA and WHO criteria would result in a considerable increase in the rate of GDM, which would lessen cases of misdiagnosis. However, increasing its prevalence does not necessarily mean better prognosis. One strength of our research is being able to use the three available criteria in the diagnosis of GDM and applying it in a good sample population. However, this research would be more significant if we were able to follow through the course of pregnancy and delivery of the mothers to monitor pregnancy outcomes. Standardizing the criteria for diagnosis will prevent pregnancy complications due to GDM. A single global criterion for the diagnosis of GDM is a must to strengthen its diagnosis and protect both the mother and the baby. Further studies on pregnancy outcomes when using IADPSG criteria may be done to determine the benefits and drawbacks of such criteria.

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